or having an IgG4 isotype. In one aspect, the peptide or protein is a monoclonal antibody or a bispecific antibody. In yet another aspect, the peptide or protein is an antibody, an antibody fragment, a Fab region of an antibody, an antibody-drug conjugate, a fusion protein, a protein pharmaceutical product or a drug.

[0011] This disclosure provides a method of producing a preparation comprising a protein of interest and a reduced amount of infectious viral particles from a sample having the protein of interest and an infectious viral particle. In some exemplary embodiments, the method of producing a preparation comprising a protein of interest and a reduced amount of infectious viral particles from a sample having the protein of interest and an infectious viral particle, comprising subjecting the sample to a pH of greater than pH of about 3.60 and ionic strength condition by addition of a salt with a concentration up to about 100 mM; and maintaining the sample at the pH and ionic strength conditions for an appropriate amount of time to produce the preparation comprising the protein of interest and the reduced amount of infectious viral particles.

[0012] In one aspect, the concentration of the protein of interest in the sample is less than about 25 g/L.

[0013] In one aspect, the appropriate amount of time is about 15 minutes, about 20 minutes, about 25 minutes, or about 30 minutes.

[0014] In one aspect, the method reduces the amount of infectious viral particles from a sample at by about 3 LRF (logarithmic reduction factor). In another aspect, the method reduces the amount of infectious viral particles from a sample at by about 4 LRF.

[0015] In one aspect, the pH condition of the sample is greater than about pH 3.70. In another aspect, the pH condition of the sample is greater than about pH 3.80. In yet another aspect, the pH condition of the sample is greater than about pH 3.90. In yet another aspect, the pH condition of the sample is greater than about pH 4.0.

[0016] In one aspect, the pH condition of the sample is in a range of from about pH 3.60 to about pH 4.0. In another aspect, the pH condition of the sample is in a range of from about pH 3.70 to about pH 4.0. In yet another aspect, the pH condition of the sample is in a range of from about pH 3.80 to about pH 4.0.

[0017] Exemplary sources for a "sample" may include an affinity chromatography, such as Protein A eluate; the sample may be obtained from a flow-through fraction of ion exchange chromatography procedure; it may also be obtained from the strip of an ion exchange column—there are other sources during a purification process well known to those skilled in the art from which a sample may be obtained. In one aspect of this embodiment, the sample is an eluent from protein A chromatography.

[0018] In one aspect, the ionic strength of the sample is adjusted by using an addition of sodium chloride, wherein a concentration of the sodium chloride is in a range of from about 1 mM to about 200 mM.

[0019] In one aspect, the ionic strength condition is adjusted by using a sodium chloride with a concentration of greater than about 50 mM. In another aspect of this embodiment, the concentration is greater than about 100 mM.

[0020] In one aspect, the pH condition of the sample is adjusted using phosphoric acid or glycine HCl.

[0021] These, and other, aspects of the invention will be better appreciated and understood when considered in conjunction with the following description and the accompanying drawings. The following description, while indicating various embodiments and numerous specific details thereof, is given by way of illustration and not of limitation. Many substitutions, modifications, additions, or rearrangements may be made within the scope of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] FIG. **1**A shows the adjust-spike-readjust method, wherein samples are adjusted/titrated to the target pH then spiked with the virus stock at about pH 7.2 followed by readjusting the pH of the samples to the target pH prior to being held at the desired temperature for the remainder of the pH hold according to an exemplary embodiment. Timing begins at the time of the spike.

[0023] FIG. **1**B shows the spike-adjust method, wherein samples are first spiked with the virus stock solution then adjusted/titrated to the target pH according to an exemplary embodiment. Timing begins at the time the target pH of the sample is reached.

[0024] FIG. **2**A shows the scatterplot matrix and multivariate correlations of the D-optimal model design to investigate the effects of several factors associated with the low pH hold step for virus inactivation according to an exemplary embodiment.

[0025] FIG. **2**B shows the neutral controls which were performed for each monoclonal antibody salt condition. The purpose of this control is to ensure that the measured viral activity was a result of chemical inactivation at low pH according to an exemplary embodiment.

[0026] FIG. **3**A shows inactivation kinetics of X-MuLV at target pH 3.65 according to an exemplary embodiment. LRF curves at target pH 3.65 were obtained by plotting LRF values against time points according to an exemplary embodiment.

[0027] FIG. **3**B shows inactivation kinetics of X-MuLV at target pH 3.73 according to an exemplary embodiment. LRF curves at target pH 3.73 were obtained by plotting LRF values against time points according to an exemplary embodiment.

[0028] FIG. **3**C shows inactivation kinetics of X-MuLV at target pH 3.80 according to an exemplary embodiment. LRF curves at target pH 3.80 were obtained by plotting LRF values against time points according to an exemplary embodiment.

[0029] FIG. **4**A shows inactivation kinetics of X-MuLV at 0 mM NaCl at different target pH conditions, for example, about pH 3.65, pH 3.73, or pH 3.80, according to an exemplary embodiment. LRF curves were obtained by plotting LRF values against time points for different target pH conditions according to an exemplary embodiment.

[0030] FIG. **4**B shows inactivation kinetics of X-MuLV at 50 mM NaCl at different target pH conditions, for example, about pH 3.65, pH 3.73, or pH 3.80, according to an exemplary embodiment. LRF curves were obtained by plotting LRF values against time points for different target pH conditions according to an exemplary embodiment.

[0031] FIG. **4**C shows inactivation kinetics of X-MuLV at 100 mM NaCl at different target pH conditions, for example, about pH 3.65, pH 3.73, or pH 3.80, according to an exemplary embodiment. LRF curves were obtained by plotting LRF values against time points for different target pH conditions according to an exemplary embodiment.